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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,902	12/17/2003	David Brown	P24170	4047

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EXAMINER	
SHEIKH, HUMERA N	

ART UNIT	PAPER NUMBER
1615	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
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Office Action Summary	Application No.	Applicant(s)	
	10/736,902	BROWN ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-74* is/are pending in the application.

4a) Of the above claim(s) *25,26 and 39-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24,27-38 and 68-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/15/04;5/16/05;2/7/06;* 10/27/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of the Response to Restriction/Election and Applicant's Arguments/Remarks, both filed 05/04/07 and the Information Disclosure Statements (IDS) filed 10/15/04, 05/16/05, 02/07/06 and 10/27/06 is acknowledged.

Applicant's election with traverse of Group I (claims 1-59 & 68-74) in the reply filed on 05/04/07 is acknowledged. The traversal is on the ground(s) that "The searches for inventions I-III should significantly overlap, if not be substantially coextensive and thus, there is no serious search burden". This is not found persuasive because, as stated in the Restriction requirement, Group I is drawn to product claims whereas each of Groups II and III are drawn to process claims. The different groups would encompass different issues relating to patentability and enablement. Moreover, the groups are different, each from the other, as evidenced by their distinct classification. Thus, the different groups would require separate searches and there is no expectation that the searches would be coextensive in scope. This creates a burdensome search upon the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

Claims 25, 26 & 39-67 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 05/04/07.

Claims 1-74 are pending in this action. Claims 25, 26 and 39-67 have been withdrawn (based on non-elected invention). Claims 1-24, 27-38 and 68-74 are being examined in this Office Action. Claims 1-24, 27-38 and 68-74 are rejected.

Inventorship

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

(1) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-98 of copending Application No. 10/798,884 ('884 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine, whereas the first drug of the copending '884 application is morphine and pharmaceutically acceptable salts thereof. However, it would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. While the '884 copending application claims a first drug being morphine derivatives having antitussive activity, it is noted that the instant application demonstrates that additional active agents, such as antitussives, can also be used in the composition (see instant claims 4 &5). Thus, there would be ample motivation to use the morphine derivatives having antitussive activity of '884 within the pharmaceutical dosage of the instant application, since the instant application recognizes that antitussives are also useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

(2) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-101 of copending Application No. 10/910,806 ('806 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine, whereas the first drug of the copending '806 application is carbetapentane and pharmaceutically acceptable salts thereof. However, it would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. While the '806 copending application claims a first drug being carbetapentane, which is a cough suppressant/expectorant, it is noted that the instant application demonstrates that additional active agents, such as expectorants can also be used in the composition (see instant claims 10-11). Thus, there would be ample motivation to use the cough suppressant/expectorant, carbetapentane of '806 within the pharmaceutical dosage of the instant application, since the instant application recognizes that cough suppressants/expectorants are also useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

(3) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-128 of copending

Application No. 10/939,351 ('351 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine, whereas the first drug of the copending '351 application is phenylepherine and pharmaceutically acceptable salts thereof. However, it would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. While the '351 copending application claims a first drug being phenylepherine, which is a decongestant, it is noted that the instant application demonstrates that additional active agents, such as decongestants (i.e., phenylepherine) can also be used in the composition (see instant claims 6-7). Thus, there would be ample motivation to use the decongestant, phenylepherine of '351 within the pharmaceutical dosage of the instant application, since the instant application recognizes that decongestants (i.e., phenylephereine) are also useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

(4) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-84 of copending Application No. 11/012,267 ('267 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine, whereas the first drug of the copending '267 application is diphenhydramine and pharmaceutically acceptable salts thereof. However, it would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. While the '267 copending application claims a first drug being diphenhydramine, which is a antihistamine, it is noted that the instant application demonstrates that additional active agents, such as antihistamines can also be used in the composition (see instant claims 8-9). Thus, there would be ample motivation to use the antihistamine, diphenhydramine of '267 within the pharmaceutical dosage of the instant application, since the instant application recognizes that antihistamines are also useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

(5) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-156 of copending Application No. 11/115,321 ('321 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine, whereas the first drug of the copending '321 application is selected from decongestants, antitussives, expectorants, analgesics and antihistamines. However, it would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. It is noted that

the instant application demonstrates that additional active agents, such as antihistamines, antitussives, expectorants and decongestants can also be used in the composition (see instant claim 2). It is also noted that the '321 copending application also claims the use of suitable antihistamines, such as promethazine (see claims 12-13 of '321). Thus, there would be ample motivation to use the antihistamine, promethazine of '321 within the pharmaceutical dosage of the instant application, and there would be ample motivation to use the antitussives, expectorants and decongestants of '321 within the instant application, since the instant application recognizes that suitable drugs (antihistamines, antitussives, expectorants, decongestants) are also useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

(6) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-44 of copending Application No. 11/102,725 ('725 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine and the first drug of the copending '725 application is also promethazine and pharmaceutically acceptable salts thereof. The claims differ in the duration of the plasma concentration range ('725 recites plasma concentration for at least about 24 hours). However, suitable plasma concentration range and

duration of therapeutic effects can be determined by one of ordinary skill in the art through routine experimentation. It is also noted that '725 claims a second further drug (see claims 16-17), as does the instant application. It would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. There would be ample motivation to use the additional drugs disclosed in the '725 application within the instant application, since the instant application recognizes the use of the same drugs and recognizes the drugs to be useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

(7) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-44 of copending Application No. 11/102,726 ('726 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine, whereas the first drug of the copending '726 application is diphenhydramine and pharmaceutically acceptable salts thereof. However, it would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. While the '726 copending application claims a first drug being diphenhydramine, which is a antihistamine, it is noted that the instant application demonstrates that additional active agents, such as antihistamines can also be used in the composition (see instant claims 8-9). Thus, there would be ample motivation to use the

antihistamine, diphenhydramine of '726 within the pharmaceutical dosage of the instant application, since the instant application recognizes that antihistamines are also useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

(8) Claims 1-24, 27-38 and 68-74 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-55 of copending Application No. 11/115,293 ('293 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because similar subject matter has been claimed in each of the copending applications.

The first drug of the instant application is promethazine, whereas the first drug of the copending '293 application is selected from decongestants, antitussives, expectorants, mucus thinning drugs, analgesics and antihistamines. However, it would be obvious to one of ordinary skill in the art to incorporate any suitable active agents that are biocompatible, each with the other. It is noted that the instant application demonstrates that additional active agents, such as antihistamines, antitussives, expectorants and decongestants can also be used in the composition (see instant claim 2). It is also noted that the '293 copending application also claims the use of suitable antihistamines, such as promethazine (see claim 2 of '293). Thus, there would be ample motivation to use the antihistamine, promethazine of '293 within the pharmaceutical dosage of the instant application, and there would be ample motivation to use the antitussives, expectorants

and decongestants of '293 within the instant application, since the instant application recognizes that suitable drugs (antihistamines, antitussives, expectorants, decongestants) are also useful in their composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-24, 27-38 and 68-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanara *et al.* (U.S. Pat. No. 6,699,502) in view of Findlay *et al.* (U.S. Pat. No. 4,650,807).

The instant invention is drawn to a pharmaceutical dosage form which comprises (a) a first drug which is at least one of promethazine and a pharmaceutically acceptable salt thereof and (b) at least one second drug, wherein the dosage form provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70 % of a period over which the dosage form provides a plasma concentration within a therapeutic range of the first drug.

Fanara *et al.* ('502) teach oral pharmaceutical compositions for controlled release of active substances, whereby the compositions include multi-layered formulations. The compositions can be administered in a few daily doses, ideally in a single daily dose (see column 1, lines 5-13 and Abstract). The release of active substances during oral administration can be controlled by means of matrix-type pharmaceutical compositions (col. 1, lines 14-16).

According to Fanara, it is increasingly therapeutically advantageous to be able to simultaneously administer by the oral route an active substance released immediately after administration, and the same or a second active substance released gradually and regularly after administration. In the case where an active substance is released immediately and another active substance is released gradually, this makes it possible to obtain combined therapeutic effects by means of two active substances having very different pharmacokinetic profiles (col. 2, lines 36-50).

The compositions allow regular and continuous release of active substances over periods of at least 12 hours (col. 3, lines 28-31).

The controlled release compositions can be used in combination with an immediate release pharmaceutical composition for the same or for another active substance, in a single unit intended to be administered orally (col. 2, lines 32-37).

Suitable active substances disclosed include antihistamines, analgesics, antitussives and the like (col. 4, lines 57-58). Specific active substances taught include decongestants, such as pseudoephedrine, phenylepherine, phenylpropanolamine and antitussives such as hydrocodone, codeine, morphine, their optimal isomers or pharmaceutically acceptable salts (col. 4, lines 58-67).

The pharmaceutical compositions are provided in the form of tablets, of which bi-layered and multi-layered tablets are also included (col. 5, line 15 – col. 6, line 25).

The Examples at columns 6-18 demonstrate various layered controlled release pharmaceutical compositions of the invention. For instance, Example 7 at column 12, demonstrates a double-layered tablet comprising hydrocodone bitartrate. The double layered-tablets contained 15 mg doses of hydrocodone consisting of a controlled-release layer containing a 10 mg dose of hydrocodone and an immediate-release layer containing a 15 mg dose of hydrocodone. The results showed that 35% of hydrocodone was already released after 1 hour, which corresponds to the hydrocodone content in the immediate release layer (33.3% of the total dose). The release of the hydrocodone continued gradually and regularly (col. 12, line 24 – col. 13, line 26).

With respect to the instant claim limitation of the "dosage form providing a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70% of a period over which the dosage form provides a plasma

concentration within a therapeutic range of the first drug", it is the position of the Examiner that the Fanara reference meets these claim limitations. The Fanara reference explicitly recognizes and teaches simultaneous administration of multiple active agents whereby it is possible to combine therapeutic effects of active substances having very different pharmacokinetic profiles. Thus, the Fanara reference teaches an objective similar to that being claimed by Applicant.

With regards to the plasma half-lives claimed, it is noted that the Fanara reference teaches similar active ingredients as claimed and thus, the plasma half-lives would be expected to be the same as that claimed herein by Applicant.

Regarding the limitation of the 'tablet comprising a matrix with the first drug and particles which comprise the second drug', the Examiner points out that Fanara teaches the use of layered, both bi-layered and multi-layered tablets and thus, this limitation is also met by the primary reference.

Fanara *et al.* teach antihistamines (col. 4, line 58). Fanara et al. do not teach the antihistamines promethazine and chlorpheniramine and do not teach the antitussive-expectorant, guaifenesin.

Findlay *et al.* ('807) teach antihistaminic compositions, which can be in the form of tablets (col. 1, lines 6-25); (col. 5, lines 33-50). Suitable antihistamines taught include *pheniramines and promethazine* (col. 1, lines 26-31). Findlay *et al.* teach that the active compound may be formulated with a sympathomimetic agent such as decongestants (pseudoephedrine, phenylpropanolamine), an antitussive (i.e., codeine), an analgesic, anti-inflammatory or an antitussive-expectorant such as *guaifenesin* (col. 5, lines 1-21). The

compositions are free from sedative effects and have little or no anticholinergic effects (Abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the suitable antihistamines and expectorants taught by Findlay *et al.* within the formulations of Fanara *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Findlay et al. teach antihistamines, such as pheniramines and promethazine and antitussive-expectorants, such as guaifenesin, which are useful for their histamine-blocking and cough suppressing properties. The expected result would be an improved formulation for the treatment of cough suppression and allergic conditions.

With regards to particular amounts of active agents, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

* * * * *

Claims 1-24, 27-38 and 68-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fanara *et al.* (U.S. Pat. No. 6,699,502) in view of Paradissis *et al.* (U.S. Pat. No. 5,445,829).

The instant invention is drawn to a pharmaceutical dosage form which comprises (a) a first drug which is at least one of promethazine and a pharmaceutically acceptable salt thereof and (b) at least one second drug, wherein the dosage form provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70 % of a period over which the dosage form provides a plasma concentration within a therapeutic range of the first drug.

Fanara *et al.* ('502) teach oral pharmaceutical compositions for controlled release of active substances, whereby the compositions include multi-layered formulations. The compositions can be administered in a few daily doses, ideally in a single daily dose (see column 1, lines 5-13 and Abstract). The release of active substances during oral administration can be controlled by means of matrix-type pharmaceutical compositions (col. 1, lines 14-16).

According to Fanara, it is increasingly therapeutically advantageous to be able to simultaneously administer by the oral route an active substance released immediately after administration, and the same or a second active substance released gradually and regularly after administration. In the case where an active substance is released immediately and another active substance is released gradually, this makes it possible to obtain combined therapeutic effects by means of two active substances having very different pharmacokinetic profiles (col. 2, lines 36-50).

The compositions allow regular and continuous release of active substances over periods of at least 12 hours (col. 3, lines 28-31).

The controlled release compositions can be used in combination with an immediate release pharmaceutical composition for the same or for another active substance, in a single unit intended to be administered orally (col. 2, lines 32-37).

Suitable active substances disclosed include antihistamines, analgesics, antitussives and the like (col. 4, lines 57-58). Specific active substances taught include decongestants, such as pseudoephedrine, phenylepherine, phenylpropanolamine and antitussives such as hydrocodone, codeine, morphine, their optimal isomers or pharmaceutically acceptable salts (col. 4, lines 58-67).

The pharmaceutical compositions are provided in the form of tablets, of which bi-layered and multi-layered tablets are also included (col. 5, line 15 – col. 6, line 25).

The Examples at columns 6-18 demonstrate various layered controlled release pharmaceutical compositions of the invention. For instance, Example 7 at column 12; demonstrates a double-layered tablet comprising hydrocodone bitartrate. The double layered-tablets contained 15 mg doses of hydrocodone consisting of a controlled-release layer containing a 10 mg dose of hydrocodone and an immediate-release layer containing a 15 mg dose of hydrocodone. The results showed that 35% of hydrocodone was already released after 1 hour, which corresponds to the hydrocodone content in the immediate release layer (33.3% of the total dose). The release of the hydrocodone continued gradually and regularly (col. 12, line 24 – col. 13, line 26).

With respect to the instant claim limitation of the "dosage form providing a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70% of a period over which the dosage form provides a plasma

concentration within a therapeutic range of the first drug", it is the position of the Examiner that the Fanara reference meets these claim limitations. The Fanara reference explicitly recognizes and teaches simultaneous administration of multiple active agents whereby it is possible to combine therapeutic effects of active substances having very different pharmacokinetic profiles. Thus, the Fanara reference teaches an objective similar to that being claimed by Applicant.

With regards to the plasma half-lives claimed, it is noted that the Fanara reference teaches similar active ingredients as claimed and thus, the plasma half-lives would be expected to be the same as that claimed herein by Applicant.

Regarding the limitation of the 'tablet comprising a matrix with the first drug and particles which comprise the second drug', the Examiner points out that Fanara teaches the use of layered, both bi-layered and multi-layered tablets and thus, this limitation is also met by the primary reference.

Fanara *et al.* teach antihistamines (col. 4, line 58). Fanara et al. do not teach the antihistamines promethazine and chlorpheniramine and do not teach the expectorant, guaifenesin.

Paradissis *et al.* ('829) teach extended release pharmaceutical compositions containing both an immediate release formulation and an extended release formulation, whereby the compositions are preferably in the form of a tablet (see col. 1, lines 15-26). The compositions include pharmaceutically active compounds, such as antihistamines, antitussives, expectorants and decongestants (col. 3, lines 34-41). Suitable antihistamines taught include chlorpheniramine

maleate and promethazine. Suitable antitussive-expectorants taught include guaifenesin (col. 4, lines 39-47).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the suitable antihistamines and antitussive-expectorants taught by Paradissis *et al.* within the formulations of Fanara *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Paradissis *et al.* teach pharmaceutical compositions comprising effective antihistamines, such as chlorpheniramine and promethazine and teach antitussive-expectorants, such as guaifenesin, which are known to be useful for their histamine-blocking and cough suppressing effects. The expected result would be an enhanced formulation for treating cough and allergic conditions.

With regards to particular amounts of active agents, the Examiner points out that generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Pertinent Art:

Prior art made of record and cited of interest:

- **Shimizu *et al.*** (U.S. Pat. No. 6,586,004)

Shimizu et al. teach solid preparations comprising antihistamines, such as promethazine and chlorpheniramine maleate and antitussive-expectorants, such as guaifenesin (see col. 3, lines 13-31).

Conclusion

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours. (Wednesdays - Telework).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Humera N. Sheikh

Primary Examiner

Art Unit 1615

July 23, 2007

HUMERA N. SHEIKH
PRIMARY EXAMINER

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